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How to facilitate psychosocial adjustment in women tested for hereditary breast or ovarian cancer susceptibility? Insights from network analysis

Running title: Network analysis of psychosocial problems and coping in HBOC testing

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Abstract

Background: Increasingly complex genetics counselling requires guidance to facilitate counselees' psychosocial adjustment. We explored networks of inter-relationships among coping strategies and specific psychosocial difficulties in women tested for hereditary breast or ovarian cancer.

Methods: Of 752 counselees consecutively approached, 646 (86%) completed questionnaires addressing coping strategies (Brief-COPE) and psychosocial difficulties (PAHC) after the initial genetic consultation (T1), and 460 (61%) of them again after the test result (T2). We applied network analyses comparing partial correlations among these questionnaire scales, according to the type of genetic test – single gene-targeted or multigene panel, test result and, assessment time.

Results: Overall, 98 (21.3%), 259 (56.3%), 59 (12.8%) and 44 (9.6 %) women received a pathogenic variant (PV), uninformative negative (panel testing) (UN), variant of uncertain significance (VUS) or true negative (targeted testing) (TN) result, respectively. In most networks, connections were strongest between avoidance (e.g., giving up) and negative emotions. Cognitive restructuring (e.g., seeing in a different light) was inter-related to lower psychosocial difficulties. Avoidance and familial/social difficulties were strongly related in women receiving a PV result. Stronger inter-relationships were also noticed between avoidance and personal cancer (e.g., worried about getting cancer again) and hereditary predisposition (e.g., worry about the choice of possible preventive options) in women receiving a VUS result. Differences in the prominence of inter-relationships were observed by type of testing and assessment time.

Conclusions: Network analysis may be fruitful to highlight prominent inter-relationships among coping strategies and psychosocial difficulties, in women tested for HBOC susceptibility, offering guidance for counselling.

Keywords: Psychosocial difficulties, coping strategies, hereditary breast and ovarian cancer, genetic counselling, network analysis.

Introduction

The discovery of new cancer susceptibility genes has led to the implementation of multigene testing in clinical practice. In the context of the hereditary breast or ovarian cancer (HBOC) syndrome, testing a panel of genes increases the complexity of counselling especially because of the addition of cancer genes at moderate risk and the identification of an increased number of variants of uncertain significance (VUS) (1), both with unclear clinical recommendations (actionability) (2).

Gene panel testing is generally proposed to index cases, often affected with breast cancer and who are tested first in the family. In HBOC index case testing, possible results include a pathogenic variant (PV) on BRCA1/2 or other high/moderate-risk gene, an uninformative negative (UN) or a VUS result. An index case with a PV result may then inform her blood relatives that they present a possible genetic susceptibility to cancer. They may thus be offered single gene targeted testing, leading to a PV or true negative (TN) result.

Carriers of a BRCA1 or a BRCA2 pathogenic variant face up to 72% and 69% risk of breast cancer (BC) by age 80 years, and 44% and 17% risk of ovarian cancer (OC), respectively (3). When affected with BC, the risk is of 40% (BRCA1) and 26% (BRCA2) of developing a contralateral BC (4). Pathogenic variants identified in other genes from the panel, such as ATM, CHEK2, PALB2, BARD1 or RAD51D, are associated to moderate risk of BC (5). Clinical recommendations for BC or OC genetic risk management follow specific guidelines, which may comprise intensive surveillance or preventive surgeries (6).

In that context, women undergoing genetic testing for HBOC susceptibility experience a stressful situation due to the perceived threat to themselves and their families. A wide range of specific psychosocial difficulties is elicited in relation to the personal or familial cancer vulnerability, management of the hereditary predisposition or communication about cancer risk within the family (7-9). These difficulties may solicit various coping strategies (10-12).

How individuals cope with stressful events is broadly characterized as increased efforts or giving-up responses (13). According to Lazarus and Folkman (14), coping consists of a process of “constantly changing cognitive and behavioural efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person”. Coping responses may thus be thought to vary specifically according to individuals’ appraisals interacting with the characteristics of the situation. In the HBOC context, empirical research has shown that coping strategies could differ according to BC risk perception or worry (11, 15, 16), and clinical features, such as the BC diagnosis status (17, 18) or test result (17, 19).

Little research has focused on the role of different coping strategies in relation to the various psychosocial difficulties that arise in cancer genetics (12). Coping strategies such as avoidance (17), distraction or helplessness (16, 20), self-controlling (e.g., excessive breast self-examination) (15) or reliance on others (20) have been shown to predict increased worry and psychological distress. While most women at high genetic risk of BC do not evidence severe, enduring distress following genetic testing (20, 21), those with increased psychosocial difficulties may need further help to minimize their distress (7, 20). Psychosocial difficulties may be inter-related to coping strategies in possible feed-back loops. For example, more intense worries may elicit (in)appropriate coping strategies which in turn may cause more (or less) worrying. Identifying these possible vicious/virtuous cycles of mutual relationships may guide counselling as intervention on one element can have an impact on another.

Network analysis (NA) is a useful statistical approach to analyse the inter-relationships among elements of complex psychological phenomena (22, 23). To our knowledge, this approach, recently

applied in psychology (24), has never been used in the psychosocial field in cancer genetics. In contrast to statistical approaches such as regression analyses, which explain a specific outcome by a number of independent factors, or psychometric analyses which reveal latent unobservable variables, NA summarizes complex patterns of associations by computing conjoint inter-relationships among elements of phenomena (22). This analysis statistically determines the unique association between two elements, controlling for their associations with all the other elements (i.e., conditional dependence relationships). Moreover, NA may also be used to investigate inter-individual variability comparing networks according to the characteristics of the situation.

Hence, the main objective of this study was to estimate networks of inter-relationships among coping strategies and specific psychosocial difficulties in women undergoing testing for HBOC susceptibility. We also descriptively compared these networks according to the type of genetic testing, the test result, and the assessment timing.

Methods

This is a prospective, multicentre study was undertaken within BRIDGES research program (<https://bridges-research.eu>). The protocol was approved in France by the Comité consultatif sur le traitement de l'information en matière de recherche dans le domaine de la santé (CCTIRS: Consultative committee for information management in health research – N°16.314), in Germany by the Ethics Committee of the University Hospital of Cologne (N°16-098) and, in Spain by the Ethics Committee of the Instituto Catalán de Oncología of Barcelona (N° - PR111/16).

Counselees

From November 2016 to April 2018, women over the age of 18 years, eligible for BC risk testing according to national criteria, unaffected or affected by a non-metastatic BC were recruited at the Cancer genetic unit of Institut Curie (IC, France), Breast cancer clinic of Cologne University Hospital (CUH, Germany) and Cancer genetic unit of Barcelona Institute of Oncology (ICO, Spain). Women with a BC recurrence, a personal history of OC or a major psychiatric disorder were not included. All recruited women provided written informed consent.

Researchers explained the study objectives to the women on the day of the initial cancer genetic counselling visit and, when they agreed to participate, they were given questionnaires to fill in at home and return within two weeks (T1). Two months after the test result notification visit, they received another set of questionnaires to be filled in at home and returned within two weeks (T2). When necessary, a reminder call was made at both time-points. A sample size of 500 counselees was targeted in order to compare groups of at least 50 counselees by main genetic test results (i.e., positive, negative or VUS). Online questionnaire completion was also possible through CleanWeb TM software.

Questionnaires and data collection

Socio-demographic and clinical data were collected from counselees after the initial genetic consultation or from medical records.

Psychosocial assessment

Genetic-specific psychosocial difficulties were assessed at T1 and T2 using the 26-item 'Psychosocial Aspects of Hereditary Cancer' (PAHC) questionnaire (9) translated and empirically validated in French, German and Spanish cancer genetics settings (Brédart et al, The 'Psychosocial Aspects in Hereditary Cancer' questionnaire in women attending breast cancer genetic clinics: reliability, validity, responsiveness and interpretability across French-, German- and Spanish versions. Under review). It provides scores of increasing difficulties on a 0 to 100 scale for six domains addressing concerns about hereditary predisposition (e.g., worrying about the choice of possible preventive options), family and social issues (e.g., feelings of responsibility towards family members related to genetic testing), negative emotions (e.g., insecure about the future), familial cancer (e.g., worry that family member has cancer), personal cancer (e.g., worry about chance of getting cancer again), and children-related issues (e.g., guilt about passing genetic alteration).

Adequate internal consistencies with Cronbach's alpha > 0.70 were found for these scales in the three language versions .

Coping was measured at T1 and T2 using the Brief-COPE abbreviated inventory of coping responses (25). Available in French- (26), German- (27) and Spanish- (28) language, this 28-item measure presents fourteen 2-item scales. Following a higher order empirical validation (29), to allow a more parsimonious assessment, these scales were aggregated into five dimensions: 1) avoidance, 2) cognitive restructuring, 3) problem solving, 4) distraction and 5) support seeking. Instructions asked about the counselee's usual strategies to respond to difficult events such as the risk of cancer.

All but two of the five scales and three languages (avoidance: Cronbach's alpha=0.57 in Spanish; Distraction: Cronbach's alpha=0.58 in French) exceeded Cronbach's alpha 0.60, which is above the value of 0.50 regarded as minimally acceptable.

Statistical analyses

Statistical analyses were performed with R software (R Core Team, 2017). Network analyses were carried out with the qgraph statistical package of R software (30).

Socio-demographic, clinical and psychosocial univariate and bivariate statistics has been described previously (31).

Network analyses provide graphs which consist of two elements: nodes (circles; observed variables corresponding to the Brief-COPE and PAHC domains in orange and blue, respectively) and edges (lines; links or inter-relationships between these variables) (30, 32). The links between variables are estimated using partial correlation coefficients, controlling for all other variables. The thickness of the edge represents the strength of the inter-relationship and is proportional in absolute value to the size of the partial correlation coefficient. The stronger the link between two nodes, the thicker the edge. Positive and negative links are denoted by blue and red edges, respectively.

Networks were regularized using an algorithm called graphical LASSO ('Least Absolute Shrinkage and Selection Operator'). Graphical LASSO removes network links to obtain the simplest network that best reproduces the partial correlations matrix (fewer links and therefore easier interpretation) while losing as little information as possible (33). The regularization severity parameter was set at 0.5 to obtain highly regularized networks. Whereas potential information may be lost, the remaining links are expected to be found in another sample of observations. Nodes are organized in such a way that the variables with the most intense inter-relationships to the other variables are closer to each other

and often at the centre of the network (34). For graphs readability, only edges greater than 0.10 in absolute value (partial r) were displayed.

Network comparisons: we compared networks estimated according to the type of genetic testing (i.e., single gene-targeted or multigene panel), the test result received (i.e., PV, UN, or VUS) and, the assessment time, T1 and T2, for either PV or UN. We investigated whether the basic structures of the networks were similar by calculating the linear correlation between the strength of inter-relationships among variables in a network and those in another network. A high correlation ($r > 0.70$) between networks reflects that if the strength of a relationship between two variables is high in a network, this relationship is also strong in the other network.

Note that analyses did not comprise the PAHC children-related domains as items applied to fewer women. Besides, the TN result sample was too small ($N=44$, 9.6%) to allow for estimating networks in women receiving that test result.

Results

Sample characteristics

Socio-demographic and clinical characteristics of the sample are provided in Supplementary online material S1. Among 752 counselees consecutively approached, 646 (86%) and 460 (61%) returned the questionnaires at T1 and T2, respectively. Eligible counselees and respondents did not differ on age, parental and BC diagnosis status. Overall eligible counselees' and respondents' mean (standard deviation) age was 47.8 (11.5) and 47.7 (11.4), respectively.

Multigene panel and single gene targeted testing was performed in 508 (78.6%) and 138 (21.4%) respondents, respectively. Counselees undergoing multigene panel differed as expected to those undergoing targeted testing, in that they were older ($p < 0.001$), reported having children more frequently ($p < 0.05$), were more frequently affected by BC ($p < 0.001$), lost a family member more frequently ($p < 0.001$) and had a longer time to wait for the test result receipt ($p < 0.001$).

Among respondents at T2, networks were estimated for 98 (21.3%), 259 (56.3%), and 59 (12.8%) women who received a PV, UN and VUS result, respectively.

Psychological characteristics

The mean (standard deviation) levels of genetic-specific psychosocial difficulties (PAHC) and coping strategies (Brief-COPE) by test result and at T1 and T2 are provided in Supplementary material 2. Less than 10% item omission was present in psychosocial assessments.

Network description

Figures 1a, 1b, 2a, 2b, 2c and, provided in Supplementary material S4, figures 3a, 3b, 3c and 3d show networks of inter-relationships between coping strategies and psychosocial difficulties in women undergoing targeted or panel testing, those receiving a PV, UN or VUS result, and at T1 and at T2 in women receiving a PV or UN result, respectively.

The conceptual distinction between psychosocial difficulties and coping strategies is reflected in the global structure of all networks, as domains of each concept, represented by nodes in blue (psychosocial difficulties) or in orange (coping strategies), were more closely connected to each other.

Insert figure 1a and 1b, 2a, 2b, and 2c about here

Across networks, a striking feature was the centrality of the 'emotions' node, connected to other psychosocial difficulties and to specific coping strategies. Concentrating on inter-relationships between coping strategies and difficulties (partial $r > 0.10$), the strongest links were observed between avoidance (e.g., giving up trying to deal with it) and higher negative emotions (e.g., anxious) in seven over nine networks. Avoidance was also linked to familial and social difficulties (e.g., contacting family members about genetic testing) in five of the networks. Cognitive restructuring (e.g., seeing in a different light) was the only coping strategy related to lower psychosocial difficulties, i.e. negative emotions (partial $r = -0.12$ to -0.25), concerns about familial (e.g., worried about the chance that family members will get cancer) (partial $r = -0.13$ & -0.14) or personal (e.g., worried about getting cancer again) cancer (partial $r = -0.12$ to -0.19). Problem solving, distraction and seeking support were to a lesser extent linked to psychosocial difficulties. Partial correlations coefficients > 0.10 between coping strategies and psychosocial difficulties in Network Analyses are provided in Supplementary material S3.

Network comparison

In the following, examples of differences among networks are presented.

In women offered multigene testing, a relatively strong connection emerged between avoidance and negative emotions (partial $r = 0.21$), while in women offered targeted testing, avoidance was strongly linked to familial/social difficulties (partial $r = 0.20$). In these women, a relatively strong link was also observed between cognitive restructuring and lower negative emotions (partial $r = -0.25$) which appeared to a lesser degree in women offered panel testing (partial $r = -0.14$).

Avoidance and emotions (partial $r = 0.29$) and familial/social difficulties (partial $r = 0.26$), were strongly connected in women who received a PV result. In women who received a VUS result, avoidance was linked to difficulties about personal cancer (partial $r = 0.19$) and hereditary predisposition (e.g., worry about the choice of possible preventive options) (partial $r = 0.15$). In women receiving a UN result, avoidance was also connected to emotions (partial $r = 0.26$) which, to a lesser degree, was also linked to cognitive restructuring (partial $r = -0.17$).

When comparing networks over T1 and T2 (Figures 3a, 3b, 3c and 3d shown in Supplementary material S4), we noted, for example, in PV carriers, a strong connection between avoidance and difficulties with familial/social issues, absent at T1, was revealed at T2 (partial $r = 0.24$), while the same strong link in women with uninformative negative test result (UN) present at T1 (partial $r = 0.20$), was no longer present at T2.

Discussion

In this study, we applied NA among coping strategies and specific psychosocial difficulties in women undergoing genetic testing for HBOC susceptibility, and contrasted networks by clinical features to suggest specific further counselling needs. Extending previous studies that assessed coping strategies in relation to distress as a specific outcome (15-19), NA evidenced unique inter-relationships among various coping strategies and a comprehensive range of psychosocial difficulties relevant to the cancer genetics context (9).

Among networks drawn in this study, the 'negative emotions' node was central. This PAHC questionnaire domain evidenced high correlation to psychological distress (31) and so, among nodes which were positively correlated to negative emotions, specific coping strategies may reveal unhelpful.

Prominent inter-relationships between avoidance (e.g., giving up trying to deal with it) and, negative emotions (e.g., anxious) as well as familial/social difficulties (e.g., worried about contact with family members; feelings of responsibility; lack of support) were revealed. Although a 'distraction' coping strategy may be useful while waiting for the genetic test result (35), avoidance has been recognised as an unhelpful strategy in women affected with BC generally (13) and in those facing HBOC susceptibility specifically (15-17). In contrast, cognitive restructuring (e.g., seeing in a different light, looking at something good in what is happening, learning to live with it) was the only coping strategy that inter-related to lower psychosocial difficulties. This is in line with a decreased long-term distress in relation to coping by fostering reassuring thoughts in women from HBOC syndrome (15).

Network structures proved similar across clinical features, especially over time. However, depending on the clinical situation, specific variations could be observed. For example, a relative strong link between avoidance and familial/social difficulties was revealed in women undergoing targeted testing. These women often unaffected with BC and surrounded by familial losses due to cancer (11) may have difficulty soliciting genetic information and support from relatives already affected with cancer.

Besides, we also evidenced relatively strong connections between avoidance and familial/social difficulties in women who received a PV result, which suggests that among PV carriers, those who use avoidance to cope may need further help to address their difficulties in communicating about the genetic cancer predisposition with concerned family members (36).

Moreover, links between avoidance and, hereditary predisposition difficulties (e.g., worried about coping with the test result) or personal cancer (e.g., worried about getting cancer again) emerged in women who received a VUS result. The disclosure of an ambiguous test result with a lack of actionability may be difficult to understand, maintain uncertainty and distress (37) and require further counselling to interpret the significance of this result in the context of personal or familial cancer history (38).

Referring to coping flexibility (39) or the ability to modulate the choice of coping strategies according to the situation, Bennett (12) observed that individuals attending cancer genetic counselling generally used cognitive restructuring in response to concerns they could not change, and support seeking to gain information. Similarly, we observed an inter-relationship between cognitive restructuring and negative emotions in women who learn that they did not carry a pathogenic variant whereas this link was not present in these women before obtaining their test result. The information gained from the test result, i.e. the absence of an identified pathogenic variant

explaining their personal or familial cancer history, also means that the cancer risk estimated by the family pedigree has not been clarified by genetic testing and therefore the medical recommendation remains unchanged. This situation may have prompted an acceptance mode of coping in facing one's personal cancer concerns.

A relatively smaller link between the problem solving strategy and difficulties related to hereditary predisposition was evidenced in women who received a PV. This test result may raise concerns about the choice of possible cancer risk management strategies and thus efforts to actively manage the stress associated to the confirmed high cancer risk.

Limitations and strengths

This study is the first to use NA in the psychosocial field in cancer genetics, providing nuanced information on the link between coping strategies and genetic-specific psychosocial difficulties. It comprises a relatively large sample with a high initial response rate and absence of statistical difference between respondents and non-respondents on available characteristics. However, findings are only valid to women opting for genetic testing and who were mainly affected with breast cancer. While causal relationships between strongly inter-related variables may be advocated, the direction in the relationships among coping strategies and difficulties may not be ascertained by cross-sectional analyses.

Conclusions

NA was fruitful to highlight prominent mutual relationships among coping strategies and specific psychosocial difficulties in women tested for HBOC susceptibility. These findings suggest further areas for counselling. In particular, women undergoing single gene-targeted testing, and in those with a PV test result - regardless of the genetic test type (single gene-targeted or multigene panel test), may need help to overcome avoidance and their difficulties in contacting family members. Women carriers of a PV may also need further support to make a decision about their cancer risk management. Cognitive restructuring should be facilitated, especially since as it was related to less negative emotions, personal and familial cancer worries.

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Competing interests

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Figure 1a & 1b. Networks of relationships among coping strategies and psychosocial difficulties in women undergoing targeted or gene panel testing for high breast cancer risk

Figure legend. P1 Hereditary Predisposition. P2 Familial & Social Issues. P3 Emotions. P4 Familial Cancer. P5 Personal Cancer. B1 Avoidance. B2 Cognitive Restructuring. B3 Problem Solving. B4 Distraction. B5 Seeking Support. Linear correlation between networks' coefficients for women proposed a diagnostic gene panel or predictive testing: $r=0.62$.

Figure 2a. 2b & 2c. Networks of relationships among coping strategies and psychosocial difficulties in women receiving a pathogenic variant, an uninformative negative or a variant of uncertain significance

Figure legend. Same as for fig 1. Linear correlation between networks' coefficients for women having received a pathogenic variant or a negative uninformative result: $r=0.60$; linear correlation between networks' coefficients for women having received a pathogenic variant or a variant of uncertain significance result: $r=0.59$; linear correlation between networks' coefficients for women having received a negative uninformative or a variant of uncertain significance result: $r=0.71$.

Figure 1a. Targeted testing

Figure 1b. Panel testing

Note: Linear correlation between partial correlation coefficients of networks drawn for samples of women undergoing targeted and multigene testing = $r = 0.62$

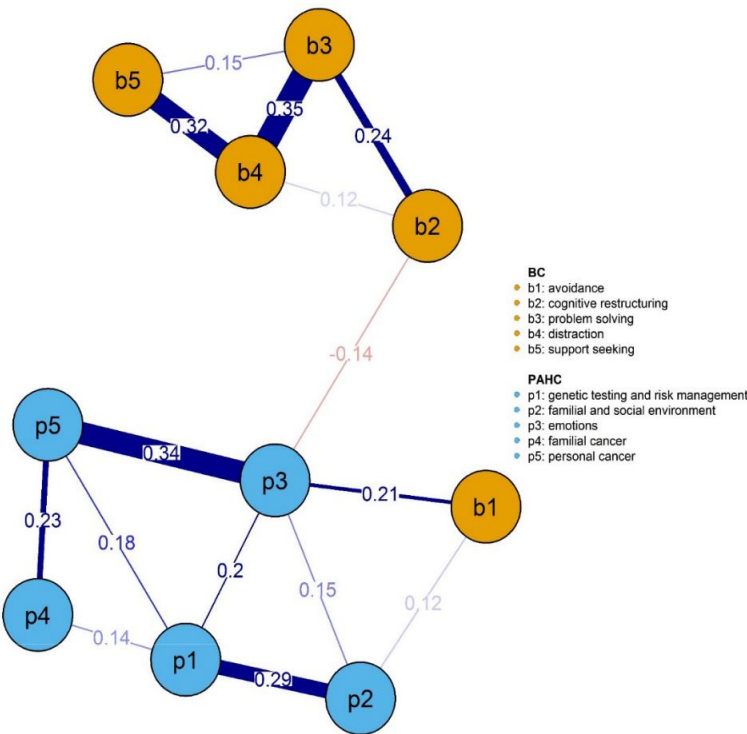
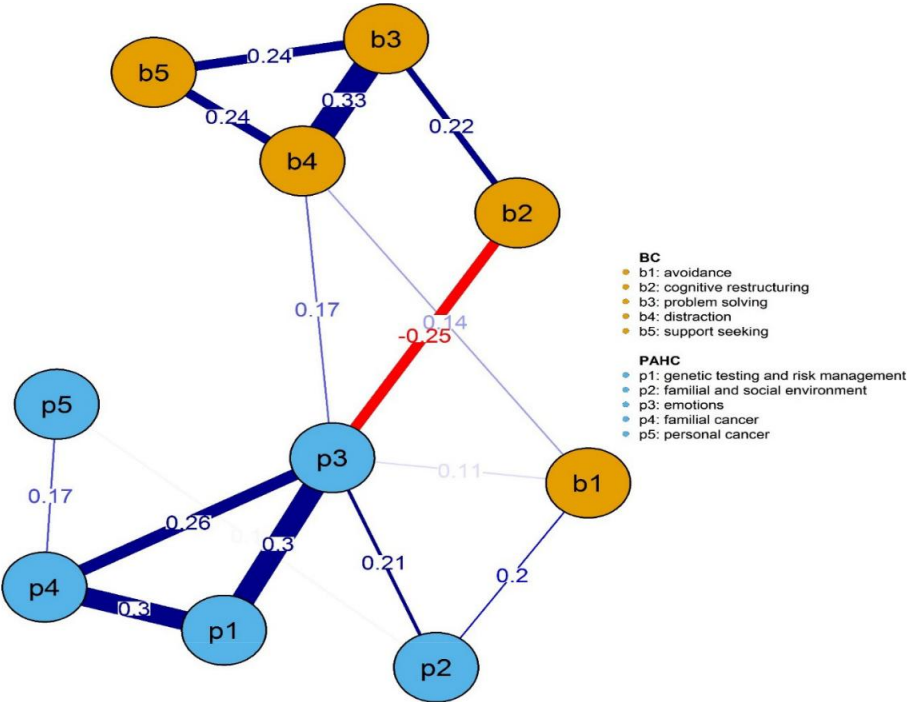
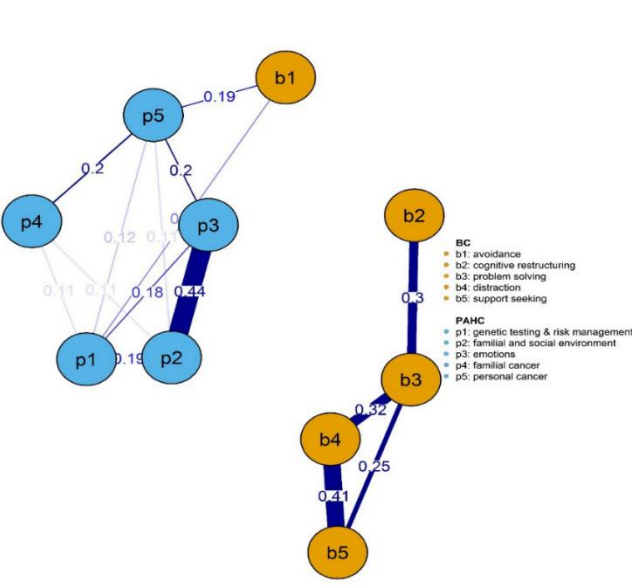
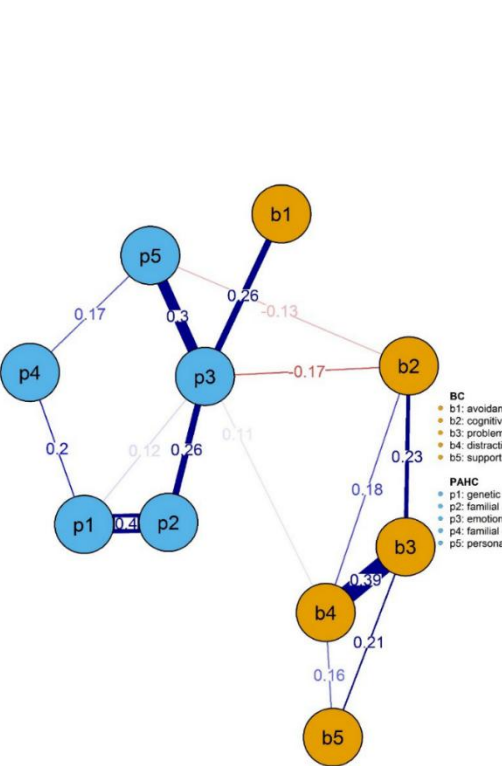
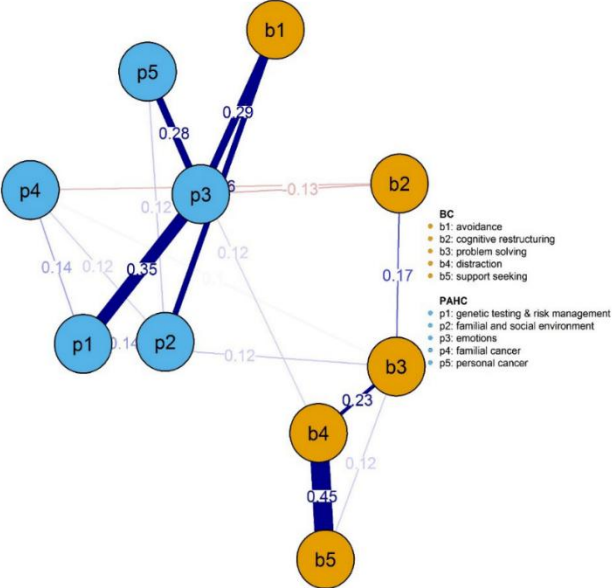


Figure 2a. Pathogenic variant

Figure 2b. Negative non-informative

Figure 2c. Variant of uncertain significance

Note: Linear correlaions between parial correlaion coeicients of networks drawn for: 1) women receiving a PV and UN result; 2) those receiving a PV and VUS result; 3) those receiving a UN and those with a VUS result = $r = 0.60$, $r = 0.59$, $r=0.71$



Supplementary material 1. Baseline socio-demographic and clinical characteristics of study participants and by genetic test result received

	Study participants N=646	Single targeted testing N = 138	Multigene panel testing N = 508
Age (years) Mean (SD)***	47.7 (11.4)	43.7 (13.3)	48.7 (10.5)
Education level n (%)			
Compulsory education or below	88 (13.7)	27 (19.9)	61 (12.1)
Secondary or technical/vocational education	271 (42.3)	52 (38.2)	219 (43.5)
Superior education	282 (44.0)	57 (41.9)	224 (44.4)
Missing data	5	2	4
Marital status n (%) Married/partnered	463 (72.2)	93 (68.4)	369 (73.2)
Missing data	5	2	4
Having children n (%) (Yes)*	486 (75.2)	92 (67.2)	393 (77.4)
Personal breast cancer n (%) (Yes)***	510 (78.9)	18 (13.1)	492 (96.9)
Time since breast cancer diagnostic (months) Mean (SD)	33.8 (65.4)	37.0 (97.1)	33.6 (64.1)
Having lost a family member due to breast/ovarian cancer n (%) (Yes)***	274 (44.4)	80 (59.7)	194 (40.2)
Genetic test result n (%) §, ***	N=460	N=90	N=370
BRCA1/2 or other high/moderate-risk pathogenic variant (PV)	98 (21.3)	46 (51.1)	52 (14.1)
Uninformative negative (UN)	259 (56.3)	0 (0.0)	259 (70.0)
Variant uncertain significance (VUS)	59 (12.8)	0 (0.0)	59 (15.9)
True negative (TN)	44 (9.6)	44 (48.9)	0 (0.0)
Length of time between initial and genetic test result disclosure consultations (days)*** Mean (SD)	105.1 (64.4)	71.4 (37.5)	113.6 (67.0)

§ Only respondents at T2. Significant difference between type of genetic testing: * p<.05; *** p<.001.

Supplementary material 2. Genetic-specific psychosocial difficulties and coping strategies mean (standard deviation) score by genetic test result and over assessment times

	Pathogenic Variant N=98		Uninformative Negative N=259		VUS N=59		True Negative N=44	
	T1	T2	T1	T2	T1	T2	T1	T2
Psychosocial difficulties (PAHC scales)								
Hereditary predisposition (HP) * (e.g.. worried about coping with the (future) DNA test results)	33.8 (24.5)	30.3 (23.7)	31.2 (22.2)	24.0 (24.1) ^{§§§}	37.0 (25.6)	19.2 (23.0) ^{§§§}	33.1 (24.8)	23.2 (25.1) ^{§§}
Familial and social issues (FSI) (e.g.. worried about contact with family members about genetic testing)	14.4 (15.6)	19.2 (22.7) [§]	14.7 (15.6)	14.7 (18.1)	17.9 (17.8)	11.6 (16.7) [§]	9.9 (13.2)	13.5 (17.6)
Emotions (E) (e.g.. anxious)	32.8 (24.3)	32.4 (23.5)	32.1 (23.8)	30.5 (23.0)	30.3 (22.7)	29.3 (25.9)	26.7 (22.6)	22.5 (21.7)
Familial cancer (FC) (e.g.. worried about the chance that family members will get cancer)	64.0 (27.3)	63.0 (27.3)	61.7 (25.4)	59.2 (27.1) [§]	57.5 (27.8)	54.5 (30.9)	66.9 (25.5)	68.2 (28.2)
Personal cancer (PC) *** (e.g.. worried/chance of getting cancer (again))	51.6 (31.1)	51.2 (28.4)	62.1 (26.7)	58.7 (26.0) [§]	60.3 (26.1)	55.4 (28.3)	41.7 (29.5)	30.2 (27.3) [§]
Coping strategies (Brief-COPE)[§]								
Avoidance (e.g.. giving up trying to deal with it)	11.0 (2.9)	10.5 (2.9)	10.7 (2.7)	10.8 (2.6)	10.0 (2.3)	10.1 (2.2)	10.0 (2.3)	10.1 (2.8)
Cognitive restructuring *** (e.g.. seeing it in a different light. making it seem more positive)	15.0 (3.7)	15.3 (3.8)	15.6 (4.2)	15.5 (4.0)	15.0 (3.7)	14.8 (4.3)	13.4 (3.8)	12.7 (4.2)
Problem solving (e.g.. taking action to try to make the situation better)	9.8 (3.3)	9.8 (3.2)	10.7 (3.1)	10.2 (3.2) [§]	10.3 (3.2)	9.8 (3.3)	9.5 (3.0)	9.0 (3.4)
Distraction *** (e.g.. doing something to think about it less)	9.7 (2.6)	8.9 (2.6) ^{§§}	10.2 (2.5)	9.7 (2.5) ^{§§§}	8.9 (2.8)	8.6 (2.7)	8.8 (2.5)	8.0 (2.9)
Support seeking	13.5 (4.4)	12.7 (4.5)	13.9 (4.2)	13.2 (4.1) [§]	13.4 (4.6)	12.8 (4.8)	12.2 (3.7)	11.3 (3.9)

	Pathogenic Variant N=98		Uninformative Negative N=259		VUS N=59		True Negative N=44	
<i>(e.g., getting emotional support from others)</i>								

Notes: T1=assessment after the initial genetic consultation; T2= assessment two-months after the receipt of genetic test result. [§] Score ranges by scale are for avoidance: 8-32; cognitive restructuring: 6-24; problem solving: 4-12; distraction: 4-12; support seeking: 6-24; increasing value means higher frequency of coping strategy use. Significant difference between test result at T2: *p<0.05; ***p<0.001; significant difference over assessment times: [§]p<0.05; ^{§§}p<0.01; ^{§§§}p<0.001.



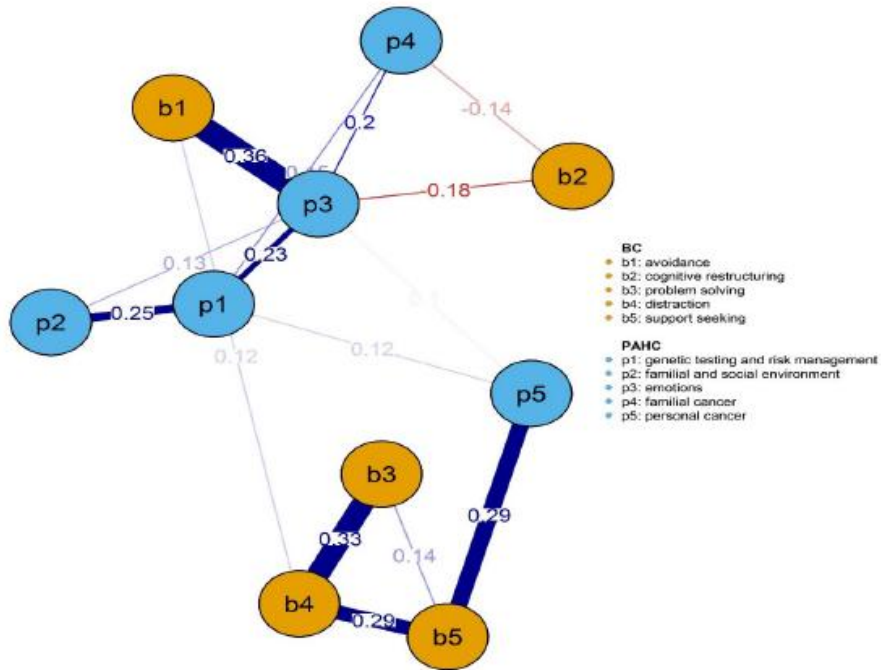
Supplementary material 3. Partial correlations coefficients > 0.10 between coping strategies and psychosocial difficulties in Network Analyses

Coping strategies by clinical context network	Psychosocial difficulties	Partial r
Figure 1a. Women undergoing single gene-targeted testing (blood relatives)		
Avoidance	Emotions	0.11
Avoidance	Familial/Social issues	0.20
Cognitive restructuring	Emotions	-0.25
Distraction	Emotions	0.17
Figure 1b. Women undergoing multigene panel testing (index cases)		
Avoidance	Emotions	0.21
Avoidance	Familial/Social issues	0.12
Cognitive restructuring	Emotions	-0.14
Figure 2a. Women with a pathogenic variant result		
Avoidance	Emotions	0.29
Avoidance	Familial/Social issues	0.26
Cognitive restructuring	Emotions	-0.13
Cognitive restructuring	Familial cancer	-0.13
Problem solving	Hereditary Predisposition	0.12
Problem solving	Familial cancer	0.10
Distraction	Personal cancer	0.12
Figure 2b. Women with a variant of uncertain significance result		
Avoidance	Hereditary Predisposition	0.15
Avoidance	Personal cancer	0.19
Figure 2c. Women with an uninformative negative result		
Avoidance	Emotions	0.26
Cognitive restructuring	Emotions	-0.17
Cognitive restructuring	Personal cancer	-0.13
Distraction	Personal cancer	0.11
Figure 3a. Women at T1 who later received pathogenic variant result		

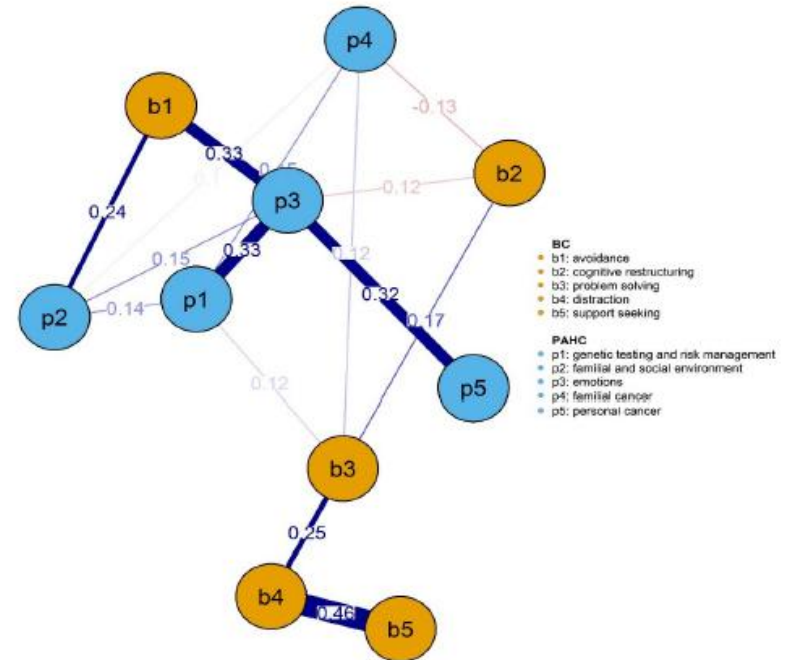
Avoidance	Emotions	0.36
Cognitive restructuring	Emotions	-0.18
Cognitive restructuring	Familial cancer	-0.14
Support seeking	Personal cancer	0.29
Figure 3b. Women with a pathogenic variant at T2		
Avoidance	Familial/Social issues	0.24
Avoidance	Emotions	0.33
Cognitive restructuring	Emotions	-0.12
Cognitive restructuring	Familial cancer	-0.13
Problem solving	Hereditary Predisposition	0.12
Problem solving	Familial cancer	0.12
Figure 4a. Women at T1 who later received an uninformative negative result		
Avoidance	Familial/Social issues	0.20
Avoidance	Emotions	0.30
Cognitive restructuring	Personal cancer	-0.19
Distraction	Familial cancer	0.11
Figure 4b. Women with an uninformative negative at T2		
Avoidance	Emotions	0.26
Cognitive restructuring	Emotions	-0.15
Cognitive restructuring	Personal cancer	-0.12

Figure 3a and 3b. Pathogenic variant at T1 and at T2

After initial consultation



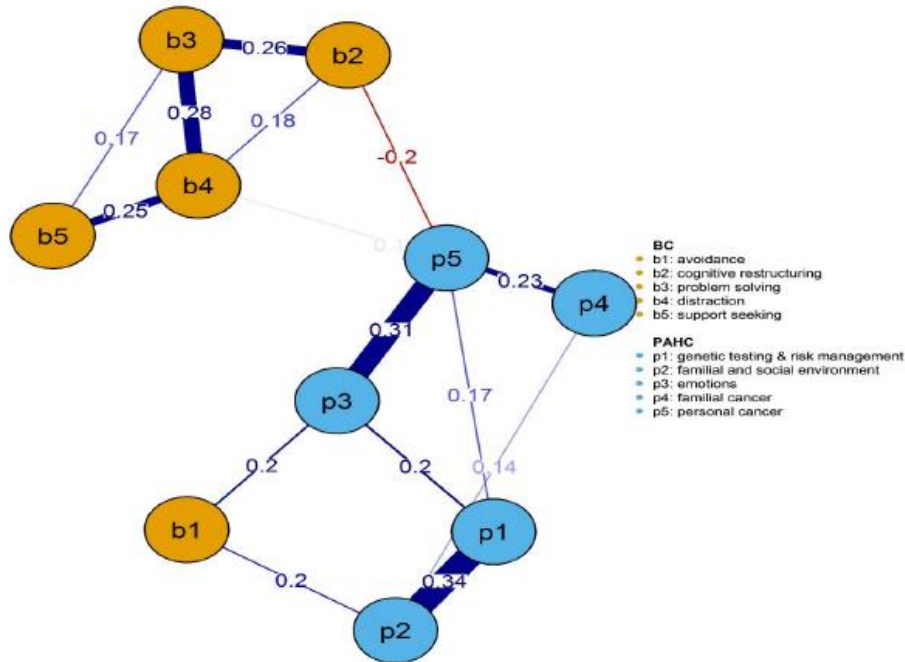
After disclosure of genetic test result



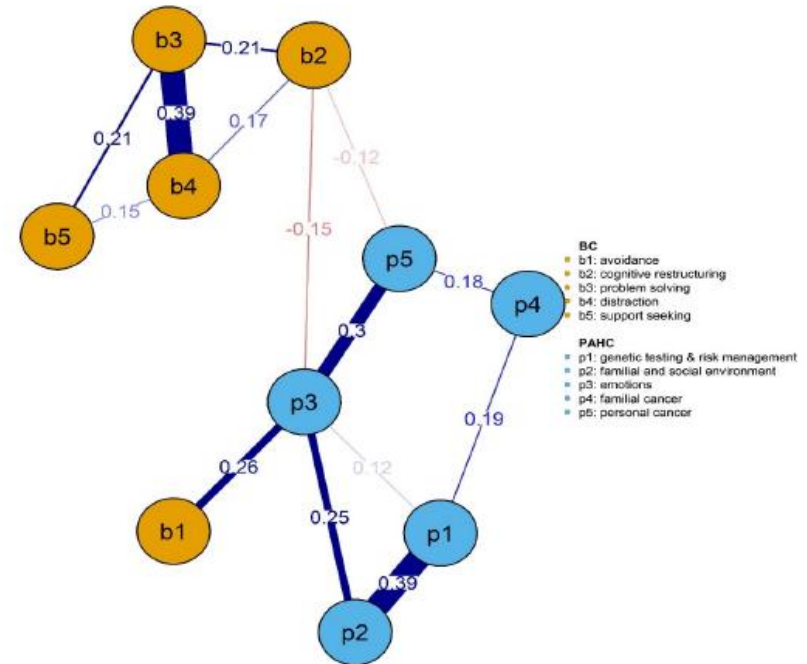
Note: Linear correlation between partial correlation coefficients of networks drawn for T1 and T2 for women receiving a PV result = $r = 0.74$

Figure 4a and 4 b. Negative non-informative at T1 and at T2

After initial consultation



After disclosure of genetic test result



Note: Linear correlation between partial correlation coefficients of networks drawn for T1 and T2 for women receiving a UN result $r = 0.82$